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Malignant transformation of the human endometrium is associated with overexpression of lactoferrin messenger RNA and protein.

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In the mouse uterus, lactoferrin is a major estrogen-inducible uterine secretory protein, and its expression correlates directly with the period of peak epithelial cell proliferation. In this study, we examine the expression of lactoferrin mRNA and protein in human endometrium, endometrial hyperplasias, and adenocarcinomas using immunohistochemistry, Western immunoblotting, and Northern and in situ RNA hybridization techniques. Our results reveal that lactoferrin is expressed in normal cycling endometrium by a restricted number of glandular epithelial cells located deep in the zona basalis. Two thirds (8 of 12) of the endometrial adenocarcinomas examined overexpress lactoferrin. This tumor-associated increase in lactoferrin expression includes an elevation in the mRNA and protein of individual cells and an increase in the number of cells expressing the protein. In comparison, only 1 of the 10 endometrial hyperplasia specimens examined demonstrates an increase in lactoferrin. We also observe distinct cytoplasmic and nuclear immunostaining patterns under different fixation conditions in both normal and malignant epithelial cells, similar to those previously reported in the mouse reproductive tract. Serial sections of malignant specimens show a good correlation between the localization of lactoferrin mRNA and protein in individual epithelial cells by in situ RNA hybridization and immunohistochemistry. Although the degree of lactoferrin expression in the adenocarcinomas did not correlate with the tumor stage, grade, or depth of invasion in these 12 patients, there was a striking inverse correlation between the presence of progesterone receptors and lactoferrin in all 8 lactoferrin-positive adenocarcinomas. In summary, lactoferrin is expressed in a region of normal endometrium known as the zona basalis which is not shed

with menstruation and is frequently overexpressed by progesterone receptor-negative cells in endometrial adenocarcinomas.

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